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Passivity-based control of a bioreactor system

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This article deals with an example of advance control techniques applied to a biochemical system, the mathematical model and the constrains derived from the discrete implementation of a continuous control policy. The theory is developed on a simplified model of a bioreactor to be regulated and passivity-based control is used. The biological interpretation of the results derived from the mathematical model takes into account the time required for chemical processes in order to obtain cells and nutrients.

KEY WORDS: bioreactor, nonlinear systems, passivity-based control

AMS subject classification: 93B12, 93C95, 34H05

1. Introduction

It is well known the wide range of applications of control theory and mathematical modelling; so, it seems useful, to check new control theories on real life problems taken from different subject areas.

This article deals with an example of application of nonlinear control techniques in the area of chemical engineering. It is worth remarking the highly nonlinear dynamic behavior of this class of systems for which linear controller design generally fails, or shows very poor performance. This characteristic is valid even within a very small range of operation in the phase plane. Thus, advanced feedback control schemes seem to be required.

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The problem we are involved with is, basically, a regulation problem defined on a continuous stirred tank reactor containing a liquid mixture of water, nutrients and biological cells. Feed substrate is introduced into the tank where the cells mix with the substrate while the culture volume is kept constant. The problem will be solved in the framework of Passivity-Based Control (see Ortega et al. [1]).

The control of a bioreactor constitutes a challenging control problem for several reasons. Although the reactor description involves but a few variables and its behavior is easily simulated, its nonlinearity makes it difficult to control. This problem satisfies the goals of relevance to real-world problems being easy enough to check the applicability of new nonlinear control techniques. On the other hand, the regulation problem in a bioreactor has been widely treated in the literature; for instance: in [2] as a problem related to the types of equilibria in classical dynamic systems, exact input/output linearization is used in [3], while adaptive control approaches may be found in [4–7]. A flatness based approach is developed in [8]. Control schemes, based in neural networks, were presented in [9–11]. For an extensive treatment of the model and control issues for bioreactors, the reader is referred to the tutorial paper of Bastin and Van Impe [12]. It is generally accepted that improvements in bioreactor control techniques may result in significant savings to the biochemical industries and a significant improvement in productivity for large volume applications.

As far as passivity is concerned, basic definitions were introduced in the early 1970s in the work of Willems [13,14], since then, different authors has been developing the subject, namely: Vidyasagar [15] and Zames [16], Hill and Moylan [17–19], Byrnes et al. [20], Kokotovic and Sussman [21] and more recently van der Schaft [22], Ortega et al. [1] and Sira-Ramírez [23,24]. Passivity-based control (PBC) exploits the system's physical properties in connection to its energy managing and dissipation enhancement possibilities.

The outline of the paper reads as follows: section 2 is devoted to a brief summary of Passivity Based Control, energy shaping and damping injection. The bioreactor model is explained in section 3. The regulation problem is solved in section 4. Simulation results can be found in section 5 and, finally, the conclusions and a list of references close the article.

2. The "energy shaping and damping injection" control design methodology

Passivity-based control has gained increasing attention in the last decade to handle nonlinear feedback controller design strategies. The method has been summarized by Ortega et al. [1] where it is applied to a series of mechanical and electro-mechanical systems of the Euler–Lagrange type. Generally speaking, chemical and biological processes do not belong to this class of systems. It is our aim here to demonstrate that the "energy shaping plus damping injection" design methodology can also be advantageously used to efficiently regulate this class of technological systems, while respecting, from the control actions, the beneficial nonlinearities related to local or global stability. The basic idea, then, is to exploit the natural energy managing structure of the system, which, roughly speaking, can generically be identified as consisting of: a *conservative* part, which should be respected, a *dissipative* part, which is regarded as beneficial and should not be cancelled, a *destabilizing* part, whose effects need to be counteracted but without necessarily eliminating these nonlinearities, and, finally, an energy acquisition part, from where our control actions are injected into the system. By removing the effect of the destabilizing part in the instantaneous variation of the storage function and, simultaneously, improving the dissipative or damping characteristics of the system, one may, with a suitable off-lined prescribed reference trajectory, influence the system responses to follow a prescribed trajectory thus achieving a pre-specified steady state equilibrium. In this respect, one heavily relies on the minimum phase properties (or stability of the residual dynamics) of the feedback passivized system.

3. The bioreactor model

Consider a continuous bioreactor, already theoretically investigated by Agraval and others (1982) in [2]. The system consists of a tank containing a substrate and biological cells in a liquid mixture. The feed substrate is introduced into the tank where the cells mix with the substrate maintaining the volume at a fixed level by removing the tank contents at an outflow rate equal to the incoming rate. The process is characterized by X, the cell concentration, S, the substrate concentration and S_F, the feed substrate concentration, the reactor volume V, the volumetric feed flow rate F, the specific growth rate $\mu(S)$, the specific substrate consumption rate $\sigma(S)$, and the real time t. The evolution of the process is described by

$$\begin{aligned} \frac{\mathrm{d}X}{\mathrm{d}t} &= -\frac{FX}{V} + \mu(S)X, \\ \frac{\mathrm{d}S}{\mathrm{d}t} &= -\frac{F(S_F - S)}{V} - \sigma(S)X. \end{aligned} \tag{1}$$

The first equation (1) describes the evolution of the biological cells with time through the variation of $\mu(S)X$ minus the cells which escape from the tank FX/V. The second equation (1) shows the variation of substrate with time as the substrate introduced minus the substrate escaping from the tank $F(S_F - S)/V$, minus the substrate consumed by the biological cells $\sigma(S)X$. The system (1) represents a model based on experimentation.

The flow rate F is the control input variable for the bioreactor. The objective of the control is to achieve and maintain the number of cells, or substrate concentration, at a desired level, starting from arbitrary initial conditions.

In accordance with the substrate inhibition and the notation used in Anderson and Miller [25], let us consider the following dimensionless variables: x_1 is the normalized cell concentration and x_2 is the substrate conversion, which will be called, normalized nutrients concentration,

$$x_1 = \frac{X}{Y(S_F)S_F},$$
$$x_2 = \frac{(1-S)}{S_F}.$$

The input variable is u, which is related to the flow through the tank,

$$u = \frac{F/V}{\mu(S_F)}.$$

Two new parameters, β and γ, appear when the substrate inhibition model is considered. The normalized system which describes the bioreactor is then:

$$\begin{aligned} \dot{x}_1 &= -x_1 u + x_1(1-x_2)\mathrm{e}^{x_2/\gamma}, \\ \dot{x}_2 &= -x_2 u + x_1(1-x_2)\mathrm{e}^{x_2/\gamma}\tfrac{1+\beta}{1+\beta-x_2}, \end{aligned} \tag{2}$$

where the output variable may be considered to be either x_1 or x_2.

In the stated case, $(1-x_2)\mathrm{e}^{x_2/\gamma}$ is the normalized specific growth rate, while $(1-x_2)\mathrm{e}^{\frac{x_2}{\gamma}}(1+\beta)/(1+\beta-x_2)$, is the normalized nutrients consumption rate, and t^* is the dimensionless time, which verifies

$$t^* = t\,\mu(S_F). \tag{3}$$

Some constraints must be considered. Cell and nutrient amounts belong each to the interval, [0, 1], i.e., $(x_1, x_2) \in [0,1] \times [0,1]$. The input variable is positive and less than or equal to 2, $\omega \in [0,2]$, the growth rate parameter is $\gamma = 0.48$ and, according to [25], the nutrient inhibition parameter is $\beta = 0.02$.

3.1. Generalities of passivity-based control

We consider systems of the form

$$\begin{aligned} \dot{x} &= f(x) + g(x)u, \quad x \in R^n, \quad u \in R, \\ y &= h(x), \quad y \in R \end{aligned} \tag{4}$$

to which a positive definite energy storage function, denoted by $V(x)$, is associated. We assume that the following *transversality* condition holds locally valid in the region of operation of the system,

$$L_g V(x) \neq 0.$$

Also, it is assumed that the output $y = h(x)$ is locally nonzero in this region.

The time derivative of $V(x)$, along the controlled solutions of the system, is given by

$$\dot{V} = L_f V + u L_g V = L_g V \left(u + \frac{L_f V}{L_g V} \right).$$

Consider the following locally invertible input coordinate transformation:

$$u = -\frac{L_f V}{L_g V} + v \frac{h}{L_g V},$$

which makes the closed loop system lossless, as, $\dot{V} = yv$. The closed loop system is therefore given by

$$\dot{x} = f(x) - g \frac{L_f V}{L_g V} + g \frac{h}{L_g V} v.$$

It is easy to see that, after some algebraic manipulations, that the closed loop system is of the form

$$\begin{aligned} \dot{x} &= \mathcal{J}(x) \frac{\partial V}{\partial x} + \gamma(x) v, \\ y &= \gamma^T(x) \frac{\partial V}{\partial x}, \end{aligned} \tag{5}$$

where

$$\begin{aligned} \mathcal{J}(x) &= \frac{1}{2 L_g V} \left[f(x) g^T(x) - g(x) f^T(x) \right], \\ \gamma(x) &= g(x) \frac{h(x)}{L_g V(x)}, \end{aligned} \tag{6}$$

where, clearly, $\mathcal{J}(x)$ is a skew-symmetric matrix. The previous developments also allow one to envision a generalized canonical form for affine systems, which is of the Generalized Hamiltonian type including dissipation and de-stabilizing terms. Indeed the original system, with the established assumptions, is trivially equivalent to,

$$\dot{x} = f(x) - g \frac{L_f V}{L_g V} + g \frac{L_f V}{L_g V} + g(x) u, \quad y = h(x). \tag{7}$$

The input coordinate transformation $u = [h(x)/L_g V(x)] v$ and further algebraic manipulations lead to,

$$\begin{aligned} \dot{x} &= [\mathcal{J}(x) + S(x)] \frac{\partial V}{\partial x} + \gamma(x) v, \\ y &= \gamma^T(x) \frac{\partial V}{\partial x}, \end{aligned} \tag{8}$$

where

$$\begin{aligned}\mathcal{J}(x) &= \frac{1}{2L_g V}\left[f(x)g^T(x) - g(x)f^T(x)\right],\\ S(x) &= \frac{1}{2L_g V}\left[f(x)g^T(x) + g(x)f^T(x)\right],\\ \gamma(x) &= g(x)\frac{h(x)}{L_g V(x)},\end{aligned} \tag{9}$$

where clearly $\mathcal{J}(x)$ is a skew-symmetric matrix and $S(x)$ is a symmetric matrix of, generally speaking, indefinite sign. Our assumptions imply that $L_\gamma V \neq 0$. Notice that the partial feedback control law:

$$v = -\left(\frac{1}{L_\gamma V(x)}\right)\left[\left(\frac{\partial V}{\partial x^T}\right) S(x)\left(\frac{\partial V}{\partial x}\right)\right] + \vartheta,$$

produces, again, a lossless system from the input ϑ towards the output y. Thus, without loss of generality we can assume that $S(x) = 0$.

Consider energy storage functions, $V(x)$, whose gradient satisfies the following *linear property* (in fact, any positive definite quadratic function of the state qualifies as such):

$$\frac{\partial V(x)}{\partial x} - \frac{\partial V(x|_d)}{\partial x|_d} = \frac{\partial V(e)}{\partial e},$$

with $e = x - x|_d$ being a “tracking error” and $x|_d$ is an auxiliary state vector which is to be designed so that the (passive) output of the system, $y = h(x)$, tracks a designed trajectory.

Consider then, over the class of derived lossless Generalized Hamiltonian systems, the stabilization of the tracking error by means of Lyapunov stability theory. i.e., let $V(e) = V(x - x|_d)$ be, as before, a positive definite storage function of e. Then

$$\begin{aligned}\dot V(e) &= \frac{\partial V(e)}{\partial e^T}\left[\mathcal{J}(x)\frac{\partial V}{\partial x} + \gamma(x)v - \dot x|_d\right]\\ &= \frac{\partial V(e)}{\partial e^T}\left\{\mathcal{J}(x)\frac{\partial V(e)}{\partial e} + \gamma(x)v + \mathcal{J}(x)\frac{\partial V(x|_d)}{\partial x|_d} - \dot x|_d\right\}.\end{aligned}$$

Notice that if we let $x|_d$ satisfy the following damped (linear) time-varying dynamics with output equation:

$$\begin{aligned}\dot x|_d &= \mathcal{J}(x)\frac{\partial V(x|_d)}{\partial x|_d} + \mathcal{R}_I(e)\frac{\partial V(e)}{\partial e} + \gamma(x)v,\\ y_d &= \gamma^T(x|_d)\frac{\partial V(x|_d)}{\partial x|_d}\end{aligned} \tag{10}$$

with, $\mathcal{R}_I(e)$, being a strictly positive definite symmetric matrix, which is a function of the tracking error e alone. We obtain:

$$\dot{V}(e) = \frac{\partial V(e)}{\partial e^T}\left[\mathcal{J}(x) - R_I(e)\right]\frac{\partial V(e)}{\partial e} = -\frac{\partial V(e)}{\partial e^T} R_I(e) \frac{\partial V(e)}{\partial e} < 0$$

and, hence, the tracking error, e, asymptotically converges to zero and the state x tracks the controlled state $x|_d$. As a consequence, the output of the system, $y = h(x) = \gamma^T(x)[\partial V/\partial x]$, also tracks the auxiliary output, $y_d = h(x|_d) = \gamma^T(x|_d)$ $[\partial V(x|_d)/\partial x|_d]$. The control of the linear time-varying system (10) is performed so that the output y_d tracks a desired output trajectory, $y^*(t)$. This can be achieved by straightforward inversion of (10). The corresponding time-varying *residual dynamics* of such an auxiliary system, evidently, qualifies as the state of the dynamic feedback controller. The feedback passivity of the original system, and of the auxiliary system, guarantee the minimum phase properties of such a residual dynamics. The obtained dynamic output tracking controller is, therefore, stable.

4. Passivity-based controller design

With $f(x) = x_1(1 - x_2)e^{x_2/\gamma}(1, (1+\beta)/(1+\beta - x_2))^T$, $g(x) = (-x_1, -x_2)^T$ and $h(x) = x_1$, the previous system is of the form,

$$\begin{aligned} \dot{x} &= f(x) + g(x)u, \\ y &= h(x). \end{aligned} \tag{11}$$

We consider the storage function $V(x)$ given by

$$V(x) = \tfrac{1}{2}(x_1^2 + x_2^2).$$

The storage function directional derivative $L_g V(x)$ along the control input vector field $g(x)$ is given by

$$L_g V(x) = -(x_1^2 + x_2^2),$$

which is not zero everywhere in $[0, 1] \times [0, 1]$ except on the point $(x_1, x_2) = (0, 0)$, which does not interest us. Thus, the operating region may be constituted by the following set

$$X = [0, 1] \times [0, 1] - \{(0, 0)\}.$$

The equilibrium points of the system (2) are given by the solutions of the equations

$$\begin{aligned} 0 &= -x_1 u + x_1(1 - x_2)e^{x_2/\gamma}, \\ 0 &= -x_2 u + x_1(1 - x_2)e^{x_2/\gamma}\frac{1+\beta}{1+\beta - x_2}. \end{aligned}$$

This system has a trivial solution, $(x_1, x_2) = (0, 0)$, which is of no interest. The case $u = 0$ in the original system produces two trivial solutions, namely $(x_1, 1)$ and $(0, x_2)$. Assuming $x_1 > 0$, $x_2 > 0$ and $u \neq 0$, it can be proved that the equilibrium points lie on the parabola

$$x_1 = -\frac{1}{1+\beta} x_2^2 + x_2, \tag{12}$$

which has the vertex at $((1+\beta)/4, (1+\beta)/2)$ and it cuts the x_2 axis on $(0, 0)$ and $(0, 1+\beta)$ (figure 1).

We obtain the given system in the form

$$\dot{x} = [J(x) + S(x)] \frac{\partial V}{\partial x} + g(x)u,$$

where

$$\mathcal{J}(x) = \frac{-x_1(1-x_2)e^{x_2/\gamma}}{2(x_1^2 + x_2^2)} \left(x_2 - x_1 \frac{1+\beta}{1+\beta-x_2} \right) \begin{pmatrix} 0 & -1 \\ 1 & 0 \end{pmatrix}, \tag{13}$$

$$S(x) = \frac{x_1(1-x_2)e^{x_2/\gamma}}{2(x_1^2 + x_2^2)} \begin{pmatrix} 2x_1 & x_2 + x_1 \frac{1+\beta}{1+\beta-x_2} \\ x_2 + x_1 \frac{1+\beta}{1+\beta-x_2} & (1-x_2)e^{x_2/\gamma} \end{pmatrix}, \tag{14}$$

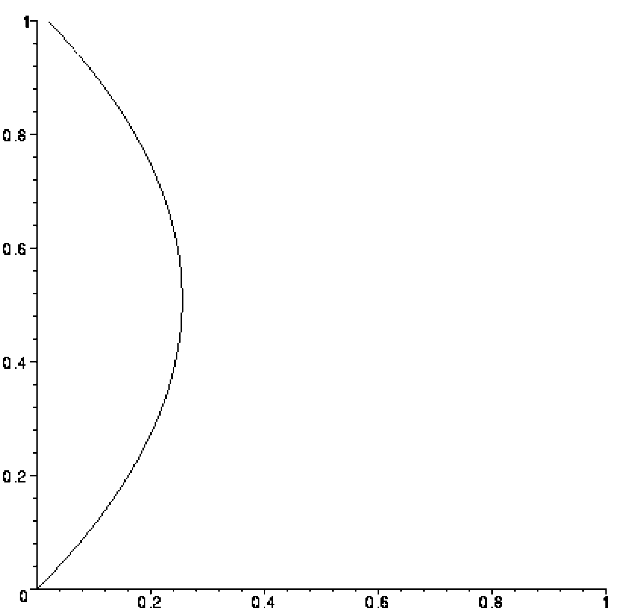

Figure 1. Parabola of the equilibrium points.

and

$$\mathcal{R}_{\mathcal{I}}(e) = \begin{pmatrix} R_1(e_1) & 0 \\ 0 & R_2(e_2) \end{pmatrix}. \tag{15}$$

The following input coordinate transformation makes the system passive with respect to the proposed storage function $V(x)$.

$$u = \frac{x_1}{x_1^2 + x_2^2}\left[(1 - x_2)\mathrm{e}^{x_2/\gamma}\left(x_1 + x_2\frac{1+\beta}{1+\beta-x_2}\right) - v\right].$$

After some simplifications the transformed system in PBCCF is given by

$$\dot{x} = -\frac{x_1(1-x_2)\mathrm{e}^{x_2/\gamma}}{(x_1^2 + x_2^2)}\left(x_2 - x_1\frac{1+\beta}{1+\beta-x_2}\right)\begin{pmatrix} 0 & -1 \\ 1 & 0 \end{pmatrix} x + \frac{x_1}{x_1^2 + x_2^2}\, x\, v. \tag{16}$$

Using the "energy shaping plus damping injection" controller design methodology, the following dynamical feedback controllers is obtained:

If $\dot{x}_2|_d = 0$ is considered

$$v = \frac{(1-x_2)\mathrm{e}^{x_2/\gamma}}{x_2}\left(x_2 - x_1\frac{1+\beta}{1+\beta-x_2}\right)x_1|_d - \frac{x_1^2 + x_2^2}{x_1 x_2}R_2(x_2 - x_2|_d)$$

with $x_1|_d$ given by the solution of

$$\dot{x}_1|_d = \frac{x_1(1-x_2)\mathrm{e}^{x_2/\gamma}}{x_1^2 + x_2^2}\left(x_2 - x_1\frac{1+\beta}{1+\beta-x_2}\right)x_2|_d + R_1(x_1 - x_1|_d) + \frac{x_1^2}{x_1^2 + x_2^2}v.$$

In order to simulate the system, we let, as in Anderson and Miller [25], the parameters γ and β to be given by: $\gamma = 0.48$ and $\beta = 0.02$.

$$\begin{aligned}
\dot{x}_1 &= -x_1 u + x_1(1-x_2)\mathrm{e}^{x_2/\gamma},\\
\dot{x}_2 &= -x_2 u + x_1(1-x_2)\mathrm{e}^{x_2/\gamma}\frac{1+\beta}{1+\beta-x_2},\\
\dot{x}_1|_d &= \frac{x_1(1-x_2)\mathrm{e}^{x_2/\gamma}}{x_1^2 + x_2^2}\left(x_2 - x_1\frac{1+\beta}{1+\beta-x_2}\right)\left(x_2|_d + \frac{x_1}{x_2}x_1|_d\right)\\
&\quad + R_1(x_1 - x_1|_d) - \frac{x_1}{x_2}R_2(x_2 - x_2|_d),
\end{aligned} \tag{17}$$

where the control input u is

$$u = \begin{cases} 0 & \text{if} \quad \omega \le 0, \\ \omega & \text{if} \quad 0 \le \omega \le 2, \\ 2 & \text{if} \quad 2 \le \omega, \end{cases} \tag{18}$$

$$\omega = \frac{x_1(1-x_2)e^{x_2/\gamma}}{x_1^2+x_2^2}\left(x_1 + x_2\frac{1+\beta}{1+\beta-x_2}\right) - \frac{x_1(1-x_2)e^{x_2/\gamma}}{x_1^2+x_2^2}\left(x_2 - x_1\frac{1+\beta}{1+\beta-x_2}\right)x_1|_d + \frac{1}{x_2}R_2(x_2 - x_2|_d).$$

5. Simulation results and conclusions

Since the actual implementation is based on a discretized system, a Zeroth Order Hold is added to the simulation. To design the sampling period we have taken into account that in chemical processes the time required for obtaining cells and nutrient concentrations can be significantly large. For the cases dealt with, a discretization step size of half an hour has been considered.

The relationship between the real time t and the dimensionless time t^* which is used in computer simulations verifies (3), where $\mu(S_F)$ can be limited by the $\mu(S)$ maximum, that is to say $\mu_{\max}$.

This value $\mu_{\max}$ appears tabulated by Heijnen and Roels [26] for different kinds of cells and substrate which verify the hypothesis of this paper. The values of $\mu_{\max}$ fulfill $0 \le \mu_{\max} \le 1$ and its average approximate value is $\overline{\mu_{\max}} = 0.25$, both in h^{-1} units.

If the $\mu_{\max}$ is 0.25 or has a relatively low value in the interval [0, 1] (this is by the far most common situation (figure 3), using a computer time $\Delta t^* = 0.125$,

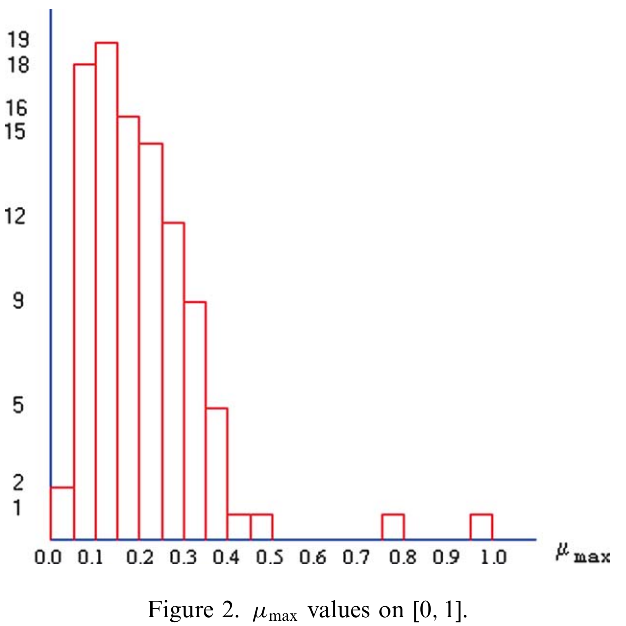

Figure 2. $\mu_{\max}$ values on [0, 1].

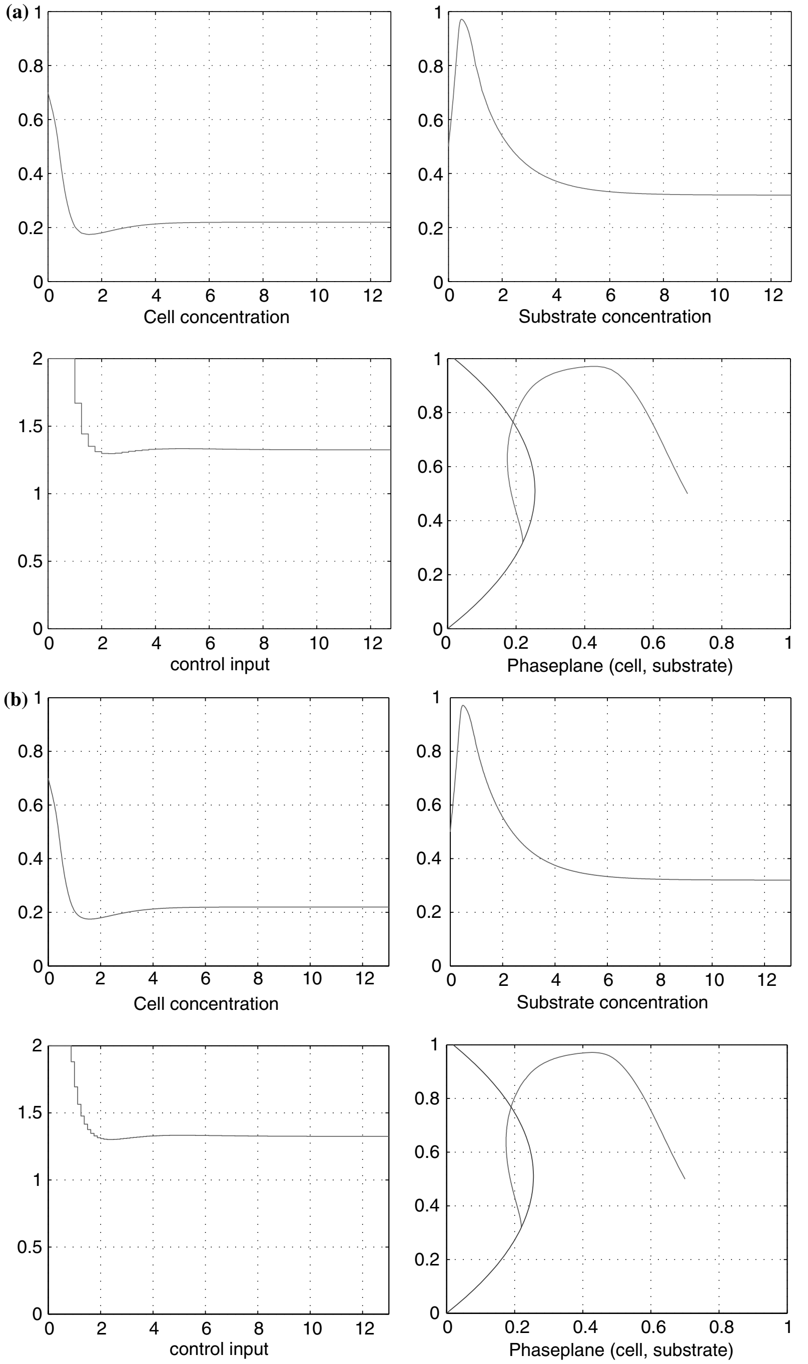

Figure 3. Discrete process of passivitation mode control with (0.2196, 0.32) destination point and $\Delta t^* = 0.125$ and $\Delta t^* = 0.25$.

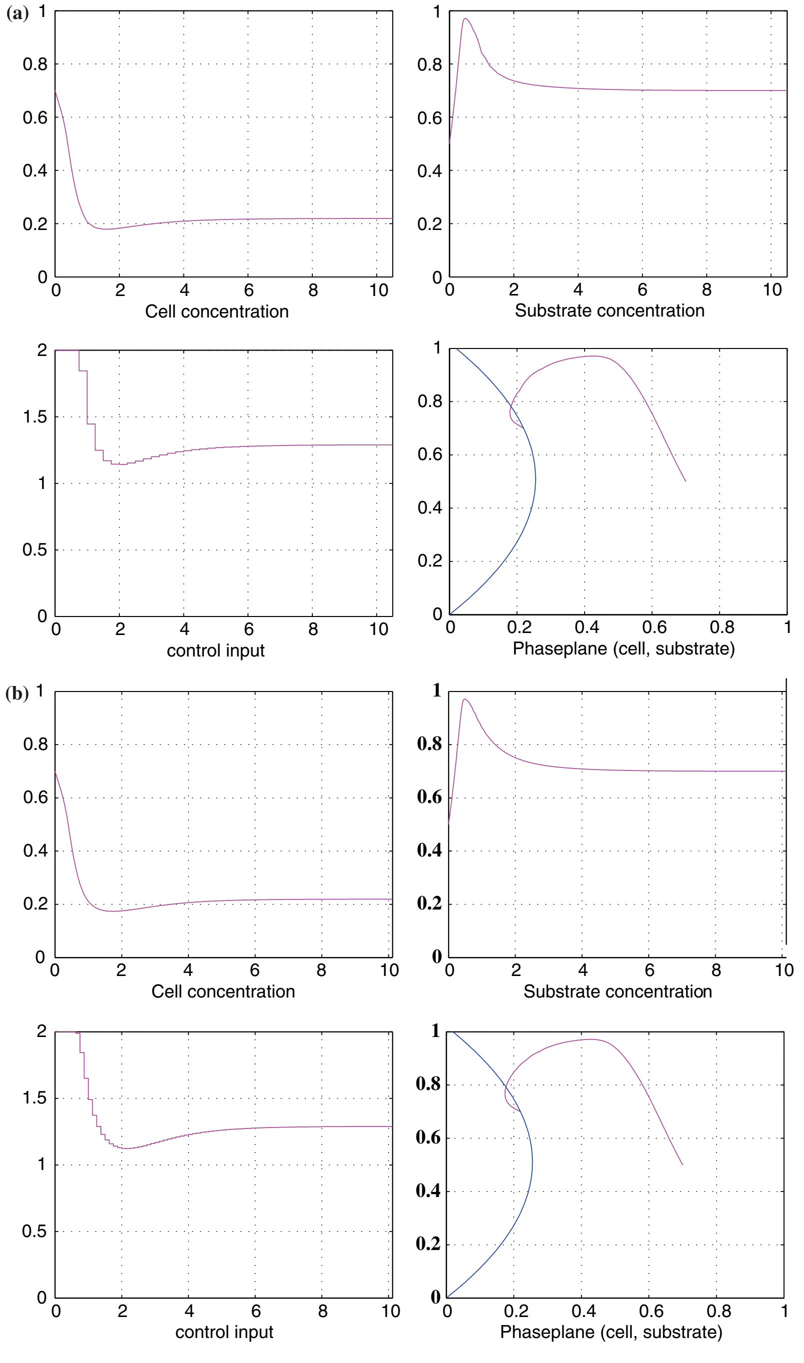

Figure 4. Discrete process of passivitation mode control with (0.2196, 0.70) destination point and $\Delta t^* = 0.125$ and $\Delta t^* = 0.25$.

corresponding to half an hour of real time, the mode control described is appropriate.

If the $\mu_{\max}$ is 1 or has a relatively high value on [0, 1] scale (which is a very unusual situation (figure 2)) and if the computer time is let to be $\Delta t^* = 0.5$, which corresponds to half an hour of real time, then the control mode presented is useful but presents some inconveniences because the control variable should be modified to a larger extent. However, the value of $\mu_{\max}$ is rarely greater than 0.5. In this case, the computer time $\Delta t^* = 0.25$ can be used with good results.

- In the discrete case, the passivization mode control presents a quick stabilization time.
- Passivization mode control provides sufficient precision for the tolerance margins used in this kind of bioreactors.

Figures 3 and 4 corroborate the previous comments. For the same cell concentration x_1, the system can be stabilized to two different nutrient concentration x_2 in the parabola of the equilibrium points. For instance, for $x_1 = 0.2196$ there are two points in the parabola, $x_2 = 0.32$ and $x_2 = 0.70$. Two simulations are presented using passivization with $x_2|d$ constant for each destination point $(0.2196, 0.32)$ and $(0.2196, 0.70)$ in figures 3 and 4, respectively. Two simulations corresponding to $\Delta t^* = 0.125$ and $\Delta t^* = 0.25$ are carried out in both cases. The resulting control input and the phase-plane graph are shown in the figures. Note the discrete implementation of the control input. However, system response trajectories appear to be continuous.

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